

two neighborhoods developed within the last 50 years were classified as W-L high wire code (6). Based on these Columbus data, if cases from the inner city are matched with controls from newer neighborhoods, odds ratios exceeding a value of 3.0 could be produced, falsely associating high wire code with childhood cancer.

Evidence exists that the cases in the 1988 Denver study may be from older neighborhoods relative to the controls. For example, of the homes classified as W-L high wire code based on secondary powerline construction, 63% of the cases and only 33% of the controls had the older "open wire" construction (7). This finding is suggestive of a failure to match cases and controls by neighborhood, which could have resulted in the creation of a false association between W-L high wire code and childhood cancer.

As compared to the W-L wire code, the authors' new wire code appears to place an even greater proportion of older powerline constructions in the high wire code category and a greater proportion of newer constructions in the low category (Table 1). Based on the authors' Table 3, the most important result may be the movement of spun wire secondaries (present standard construction which was introduced in Columbus in the 1950s) within 50 feet of a residence from the W-L "high" category to the new "low" category (23% of the W-L "high wire code" controls, while only 9% of the W-L "high wire code" cases were so reclassified). If cases are from older neighborhoods relative to the controls, application of this new wire code would likely result in a stronger but false association between the new high wire code and childhood cancer. Adjustment for age of neighborhood should remove this possible bias.

In conclusion, the fact that the new wire code is only weakly correlated with magnetic field measurements (in the same manner as the original W-L wire code) suggests that the newly reported stronger association with childhood cancer is likely due to factors other than magnetic fields. Differential residential mobility and differential residential age are two possible explanations and are suggestive that the reported association may be false.

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Response: Potential Bias in Denver Childhood Cancer Study

Jones makes several points in his letter to that we would like to address.

The observation that the modified wire code is similar to the Wertheimer-Leeper code in its relation to measured magnetic fields, yet more strongly related to cancer, is interpreted as evidence that both wire codes reflect some exposure other than magnetic fields as the basis for their relation to cancer risk, but the modified wire code does so more effectively. If the measured magnetic field were the true gold standard, this reasoning would be valid, but the real interest is in long-term, historical magnetic field exposure to occupants of the residence, which is unfortunately not available. If the modified wire code is superior, then its relation to the gold standard exposure would presumably be enhanced, but not necessarily the relation to spot magnetic-field measurements, another imperfect surrogate of exposure.

The "Back to Denver" study (1) is cited to verify that the Wertheimer-Leeper wire code can be reliably assessed. However, that study did not directly address the question of which aspects of the coding system are contributory and which are superfluous, thereby adding only random error relative to the ideal exposure measure. The greater simplicity of the new system is one of its expected contributions, allowing less skilled persons to collect valid data, but we also believe that the approach may eliminate some distinctions that are not of importance in estimating exposure. The reduction in misclassification would not be solely due to fewer actual recording errors but in more accurately and parsimoniously reflecting the field-determining characteristics of the power lines. A number of alternative explanations for the wire

code-cancer association are considered by Dovan et al. (1). Unfortunately, the data reported cannot be used to prove that magnetic fields or some factor other than magnetic fields account for the observed associations.

In a recent article (2), the hypothesis was put forth that differential residential mobility accounts for much of the association we observed originally between wire codes and childhood cancer (3). Jones et al. argue that 1) controls in our study in Denver were restricted to be residentially stable from the date of the matched case's diagnosis to the time of selection (a period of 0-9 years, depending on the corresponding case's date of diagnosis); 2) data collected in Columbus, Ohio, demonstrate an association between residential stability and wire configuration code. Occupants of homes with wire codes indicative of elevated magnetic fields are less stable; 3) application of the differential mobility by wire code in the Denver study produces an odds ratio due to selection bias of around 1.5.

Given that cases were ascertained over an 8-year period (1976-1983), which preceded data collection (1984-1985), control selection posed a challenge. If all residents of the study area at the time of selection were considered eligible, we would have included many children who had moved to the area subsequent to the corresponding case's age of diagnosis. We chose instead to restrict controls to those who were present when the case was diagnosed and remained in the area until the time of selection. We recognized that this omitted controls who would have been eligible at the time of diagnosis but who had subsequently moved away, and acknowledge that this constitutes a potentially important source of selection bias in the study (3). Data gathered by Jones et al. (2) in a different city and time period from our study provide a firmer empirical basis for such a concern, but the question of generalizability from Columbus to Denver cannot be made with certainty. Organization of cities with respect to land use, socioeconomic status, and patterns of migration are complex and quite likely to be distinctive, especially in different regions of the country.

A comprehensive analysis of our data to address the role, if any, of selection bias related to mobility is underway, but several points raised by Jones are in error. We restricted controls to be stable from the time of diagnosis to the time of selection, whereas cases were included whether stable or mobile during that period. As a result of this requirement, there was a small imbalance in the prediagnosis period (birth to diagnosis): 82 of 224 interviewed cases remained stable (37%), whereas 81 of 198

interviewed controls remained stable from birth to diagnosis (41%). Patterns of association can be examined in several ways to address this concern. The odds ratio (high versus low wire code) for children who remained stable was lower for total cancers and leukemias, but not for brain tumors (4: Table 6). More pertinent, the magnitude of any bias resulting from restricted residential mobility must be greatest for the cases diagnosed in the period most remote from the time of control selection and interview (C. Poole, personal communication), yet the odds ratios for the more recent period (1980 or later) are much larger, not smaller, than the odds ratios for the earlier period (4: Table 6). Finally, consistent with the pattern by calendar time, the wire code odds ratio for children who had magnetic field measurements (a marker of having remained residentially stable from diagnosis to selection) was 2.0 (95% CI: 1.0–3.9). For leukemia cases, the corresponding odds ratio was 3.9 (95% CI: 1.6–9.8). In fact, among cases, the proportion with high wire code was virtually identical among those who had magnetic field measurements (20%) and those who did not (19%). Perhaps in Denver, residential stability and wire configuration code are not related. Furthermore, the patterns of movement among families with children who have cancer may well differ as a result of the occurrence of the cancer, making their reasons for movement distinct from controls (C. Poole, personal communication).

The telephone exchange areas in which cases and controls were matched covered a sufficiently large geographic area to allow for disparities to occur in the wire codes. At the extreme, if the areas were sufficiently homogeneous, the cases and controls would be assured of having identical wire codes. To the extent that the random-digit dialing procedure is effective, we chose a control randomly from the same broad section of town as the case. Assuming the type of heterogeneity within areas Jones describes, the selection procedure should have provided a representative control. For his scenario of "all cases in old homes, all controls in new homes" to operate, cases would have to be unevenly distributed within telephone exchange areas, and the selection procedure would have to have been systematically biased or generated a grossly unrepresentative sample in spite of a random selection mechanism.

Jones argues that the characteristics of the secondary power line construction indicate an imbalance between cases and controls in age of neighborhood. In the original Wertheimer-Leeper coding system, homes could not be placed in the "very high current configuration" category based

on secondary lines (5), and in the modified code, secondary lines cannot result in an assignment of a home to the high level. Proximity to a primary line or transmission line is required for such a classification. The secondary power line characteristics only influence the designation as "low" versus "medium" in the modified wire code system, and because the odds ratios for the medium group were near the null, secondary power line characteristics did not have an important influence on our results.

Age of neighborhood is suggested as another potential basis for a spurious positive association. Because selection of controls was unlikely to have been biased by age of the home, Jones implies that residential age acts as a true confounder of the wire code–cancer association. Many home attributes and perhaps exposures are related to age of housing, but none are currently known to be independently related to risk of cancer in children. If, as suggested, cases tended to come from older homes than controls, an argument could be made that the association with age of residence is valid but a reflection of a causal relationship between high wire codes (associated with older homes), elevated magnetic fields, and childhood cancer.

Future studies clearly should avoid an approach to control selection that creates such an imbalance in mobility by conducting concurrent case and control ascertainment, and the data of Jones et al. (2) provide more forceful justification for doing so. Ideally, such studies would also consider potential confounders related to the neighborhood plausibly related to cancer risk. In addition to the evidence within our study results that such biases do not account for the observed associations, similar results in studies free of such potential bias (6,7) provide indirect evidence that any mobility bias is unlikely to have been substantial in the study in Denver.

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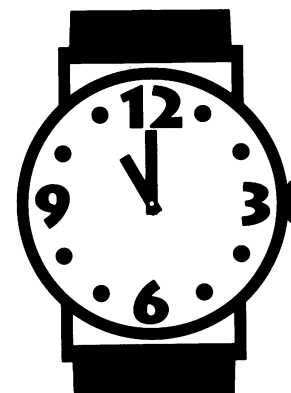
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